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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SEHARASEYON, JEGATHEESAN	
ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 10/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/928,175	PASZTY ET AL.	
	Examiner	Art Unit	
	Jegatheesan Seharaseyon	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12 and 43-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12 and 43-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This Office Action is in response to the amendment and response filed on 7/26/04. Applicant has cancelled claims 13-42 and 46-58. Claims 1-4 have been amended. Thus, claims 1-12 and 43-45 are pending and under consideration.

2. The change of title is acknowledged.

3.The text of those sections of Title 35, U. S. Code not included in this action can be found in a prior Office action.

4. Any objection or rejection of record, which is not expressly repeated in this action, has been overcome by Applicant's response and withdrawn.

Claim Objections withdrawn

5. The objection of claims 1-3 are withdrawn in light Applicants amendment.

Claim Rejections - 35 USC § 112, second paragraph withdrawn

6. The rejection of claims of claims 1-3 under 35 USC § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reciting " a nucleic acid which hybridizes under moderately or highly stringent conditions..." is withdrawn because Applicant has modified the claims to describe the specific hybridization conditions.

7. The rejection of claims of claim 8 under 35 USC § 112, second paragraph, as being indefinite for reciting a recombinant method for producing a polypeptide comprising a complementary to nucleotide sequence is withdrawn because Applicant has amended to eliminate the complementary nucleotide sequence involvement in the polypeptide making.

Claim Rejections - 35 USC § 112, second paragraph maintained

8. The rejection of claims of claims 1-3 under 35 USC § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reciting "LGR8 polypeptide" is maintained. Applicants' arguments have been fully considered but not deemed persuasive. Although, Applicant may be his or own lexicographer, Applicant fails to particularly point out and distinctly claim the "LGR8" polypeptide by sufficient identifying characteristics associated with the polypeptide. Specifically, there is no nexus between the DNA described in claims 1-3 and the LGR8 polypeptide of claim 8. Although, Applicant asserts that the specification defines LGR8 polypeptide, the specification teaches that "LGR8 polypeptide" as " a polypeptide comprising the amino acid sequence of any of SEQ ID NO: 2, 3, 5, 7, 8, 10, 12, 13, 15, 17, 18, 20, 21 or 23 and related polypeptides". Therefore, the rejection of claim 8 is maintained.

Claim Rejections - 35 USC § 101, maintained

9. Claims 1-12 and 43-45 stand rejected under 35 USC 101 for lack of utility, for reasons set forth in the Office Action of 2/25/2004. Applicant's arguments filed on 7/26/04 have been fully considered but they are not persuasive.

Applicant has traversed this rejection on the premise that the application affirmatively teaches specific nucleic acid molecules encoding polypeptides that were found to be actually expressed in animals, primarily in skeletal muscle and in the uterus. Applicants contend, therefore, that the instant application provides the public with a specific benefit (i.e., a particular member of the glycoprotein hormone receptor

subfamily). Applicant's arguments have been fully considered but are not deemed persuasive.

A nucleic acid can be patented even if it encodes no protein, provided the nucleic acid has substantial disclosed utility. When such a nucleic acid can be used as a marker for a disease or disorder or as a promoter to obtain the production of a recombinant protein in a host cell, that nucleic acid has substantial and specific utility. A protein of unknown function would also have utility if it can be employed as an indicator of a diseased state of the presence of a disorder. The only disclosed function for the protein of the instant invention, however, is as a glycoprotein hormone receptor protein. It is certain that this protein can be employed to identify compounds (ligands) which can act as agonist or antagonist of the receptor protein, but this information is without real value because the instant specification does not identify a physiological process such as blood pressure, heart rate, taste or sensation of pain which one could expect to influence by the administration of a compound that has been identified by employing a protein of the instant invention. If a protein of the instant invention was a receptor for a known glycoprotein ligand then the protein would have utility in the purification of that ligand, but the instant specification does not identify any specific ligand that is known to be bound to this receptor protein. Applicant is not being required to identify a ligand for that receptor protein, **and** a physiological process mediated thereby **and** a disease or disorder for which that protein is a marker. Applicant is only required to identify **one** specific, substantial, credible utility and, as stated in the previous Office Action, the employment of this protein only as the subject of further research does not satisfy the

utility requirement of 35 USC 101 because the courts have interpreted this statute as requiring an invention to have "substantial utility" "where specific benefit exists in currently available form" (*Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966)).

Applicant asserts that the nucleic acid molecules, or the polypeptides they encode, may be used to treat, diagnose, ameliorate, or prevent a number of diseases, disorders, or conditions associated with LGR8 polypeptides, for example using the claimed molecules to diagnose or treat diseases and conditions that modulate cellular proliferation and differentiation, such as wound healing have uses within the commercial marketplace in the drug development cycle, since they encode previously unidentified members of important pharmaceutical targets. To date, each clinical agent that has been developed by measuring its interaction with a specific receptor or transmitter was evaluated against a receptor or transmitter whose native ligand or substrate or ion and physiological function were known, such as the GABA receptors and the NMDA receptors. There are also numerous receptor proteins that do not mediate clinically significant process. More importantly, artisans knew, before they employed a specific receptor/transmitter protein to identify clinically useful compounds, which physiological process or processes they wished to manipulate and that the protein employed in their assay had an effect in that process. Even if one identifies an agonist or an antagonist for a receptor of the instant invention, this information is useless since one has no idea of what clinical effect the administration of that agonist or antagonist to an individual would have. Applicant has not shown that the claimed receptor is useful for screening drug compounds.

Applicants also assert that members of the glycoprotein hormone receptor family are well known and play an important role in multiple disease states and conditions. A member of the glycoprotein hormone receptor family has a "real world" use in binding glycoprotein ligands and thus in treating, diagnosing, ameliorating, or preventing various disease states and conditions associated with glycoprotein signaling. In addition, Applicants also discuss extensively the homology of LGR8 with LGR family. However, being a member of the LGR family of proteins does not confer (by it self) any "real world" use to nucleotides encoding the polypeptide.

To grant Applicant a patent encompassing an isolated polynucleotide encoding a naturally occurring human protein of as yet undetermined biological significance would be to grant Applicant a monopoly "the metes and bounds" of which "are not capable of precise delineation". That monopoly "may engross a vast, unknown, and perhaps unknowable area" and "confer power to block off whole areas of scientific development, without compensating benefit to the public" *Brenner v. Manson*, *ibid*). To grant Applicant a patent on the claimed polynucleotide based solely upon an assertion that the protein encoded thereby can be employed as glycoprotein hormone receptor binding potential glycoprotein ligands is clearly prohibited by this judicial precedent since the compensation to the public is not commensurate with the monopoly granted and would be no different than granting a patent on the process disputed in *Brenner v. Manson* on the premise that the steroid produced thereby was useful as an analytical standard or as a fuel source.

Claim Rejections - 35 USC § 112, first paragraph, maintained.

9. Claims 1-12 and 43-45 stand rejected under 35 USC 112, first paragraph is maintained for reasons set forth in the Office Action of 2/25/04 and paragraph 8 above. Applicant's arguments filed on filed on 7/26/04 have been fully considered but they are not persuasive.

10. Claims 1-3 stand rejected under 35 USC 112, first paragraph, as failing to comply with the written description requirement. Applicant's arguments have been fully considered but are not found to be persuasive because the Applicant has not provided evidence to demonstrate that the skilled artisan would be able to envision the detailed structure of the infinite number of polynucleotides recited in the claims.

Applicants contend that the instant Application, in combination with the knowledge already possessed by one of skill in the art, does in fact disclose relevant, identifying characteristics describe the instant invention. The description of LGR8 polynucleotide and polypeptide in the specification of the instant application is not a representative number of embodiments to support the description of an entire genus of functionally equivalent polynucleotides and polypeptides which incorporate all mutants, derivatives, variants, nucleotide sequences obtained by the hybridization and fragments having at least 70% identity to the nucleic acid sequences encoding SEQ ID NO: 2 or 3. Therefore, only an isolated nucleic acid molecule consisting of the nucleotide sequence of SEQ ID NO: 1 and a nucleic acid molecule which encodes a polypeptide consisting of the amino acid sequence of SEQ ID NO: 2 or 3, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. In addition,

the broad-brush discussion of making or screening for allelic variants does not constitute a disclosure of a representative number of members. No such variants were made or shown to have activity. The specification's general discussion of making and screening for variants constitutes an invitation to experiment by trial and error. Such does not constitute an adequate written description for the claimed variants.

Furthermore, to provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is a partial structure in the form of a recitation of percent identity and polynucleotide/polypeptide fragments and variants. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. Therefore, claims 1-3 stand rejected under 35 USC 112, first paragraph, as failing to comply with the written description requirement.

11. Claims 1-3 stand rejected under 35 USC 112, first paragraph, as being not enabled commensurate in scope with these claims. Applicant's arguments have been fully considered but are not found to be persuasive because the Applicant has not provided

evidence to demonstrate that the skilled artisan would be able without undue experimentation be able make and use the instant invention.

Despite knowledge in the art for producing variants of a given polypeptide with amino acid deletions, insertions or substitutions the specification fails to provide any guidance regarding the changes/modifications contemplated with regard to polynucleotides and polypeptides which incorporate all mutants, derivatives, variants, nucleotide sequences obtained by the hybridization and fragments having at least 70% identity to the nucleic acid sequences encoding SEQ ID NO: 2 or 3. Furthermore, detailed information regarding the structural and functional requirements of the disclosed protein is lacking. Although it is accepted that the amino acid sequence of a polypeptide determines its structural and functional properties, predicting a protein's structure and function from mere sequence data remains an elusive task. In addition, it is also unclear what regions of the polypeptide are required to confer this activity. The specification only describes SEQ ID Nos: 1-3 and fails to teach or describe any other molecules that meet the structural limitations of the claims. Since, there is inadequate guidance as to the nature of the invention, it is merely an invitation to the artisan to use the current invention as a starting point for further experimentation to try and identify the various sequences. The breadth of the claims is such that the claims encompass polynucleotides from other species and related polynucleotides that have yet to be described. There is a lack of guidance or teaching regarding structure and function of the polynucleotide because there is only the description of SEQ ID NO: 1 and

polynucleotide encoding SEQ ID NO: 2 or 3 provided in the specification and because there is no guidance found in the prior art for this specific sequences.

Applicants contend that the specification is fully enabling for fragments of the explicitly disclosed sequences (including C-and/or N-terminal truncations), as one of skill in the art would, with little effort effort, be able to create a sub-section of the explicitly disclosed sequences. However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active variants, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. Therefore, predicting which nucleotide sequence encoding the variants would retain the functions of the LGR8 protein is well outside the realm of routine experimentation. Thus, undue amount of experimentation would be required to generate

changes/modifications of the nucleotides contemplated and yet retain the function of the LGR8 variant proteins claimed.

12. No claims are allowed.

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon whose telephone number is 571-272-0892. The examiner can normally be reached on M-F: 8:30-4:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JS 10/04

Brenda Brumback

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